IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Yong Mi Choi-Sledeski, et al.**

Application No.: **Not Assigned** Examiner:

Filed: **Herewith** Group Art Unit:

For: **SULFONIC ACID OR SULFONYLAMINO N-(HETEROARALKYL)-AZAHETEROCYCLYLAMIDE COMPOUNDS**

Attorney Docket No.: **A2513 US DIV 1**

CERTIFICATE OF EXPRESS MAILING

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service on this date, **July 30, 2001** in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number EL 389265150 US addressed to: Commissioner for Patents, Washington, D.C. 20231

Dated: July 30 2001

Jaclyn M. Schlitter

Box Patent Application
Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Sir:

Please enter the following amendments prior to examination of the above-identified patent application.

IN THE SPECIFICATION

Please amend the specification as follows:

At page 1, please amend the first paragraph beginning at line 5 to read as follows:

This application is a divisional of U.S. Application No. 09/453,307, filed December 12, 1999, which is a continuation-in-part of International Application No. PCT/US99/12312, filed June 3, 1999, which is, in turn, a continuation-in-part of U.S.

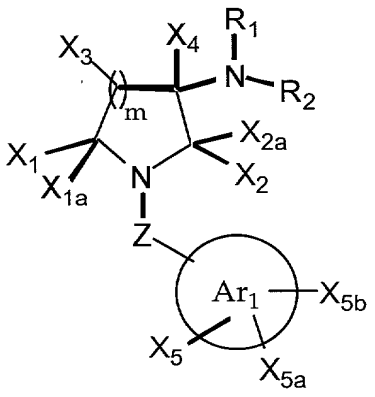
Application No. 09/090,492, filed June 3, 1998, which is, in turn, a continuation-in-part of International Application No. PCT/US97/22406, filed December 3, 1997, which, in turn, claims priority benefit of U.S. Provisional Application No. 60/033,159, filed December 13, 1996, the disclosures of all of which are incorporated herein by reference.

IN THE CLAIMS

Please cancel claims 3-5, 7, 13, 15 to 21 and 42, without prejudice.

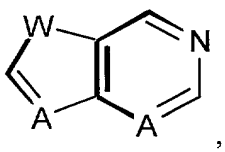
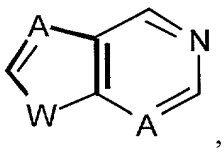
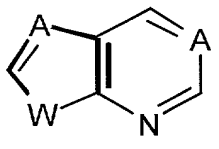
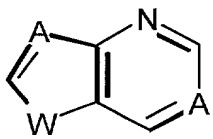
Please amend claims 1, 2, 8, 11, 12, 22, 23 and 25-29 as follows:

1. (Amended) A compound of formula I



(I)

wherein  is an optionally substituted moiety of formula


, 
, 
, or 

in which W is NR_{11}, wherein R_{11} is H, alkyl, aralkyl, heteroaralkyl or $R_8(O)CCH_2$-, and A is CH;

Z is alkylenyl, $-(CH_2)_rC(O)NR''(CH_2)_s-$, $-(CH_2)_sR''NC(O)(CH_2)_r-$ or $-(CH_2)_sNR''(CH_2)_r-$;

R_1 is hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aralkyl, substituted aralkyl, heteroaralkyl, substituted heteroaralkyl, $R'O(CH_2)_X$-, $R'O_2C(CH_2)_X$-, $R'C(O)(CH_2)_X$-, $Y^1Y^2NC(O)(CH_2)_X$- or $Y^1Y^2N(CH_2)_X$-;

R' and R" are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aralkenyl, substituted aralkenyl, heteroaralkenyl, substituted heteroaralkenyl, aralkyl, substituted aralkyl, heteroaralkyl or substituted heteroaralkyl;

R_2 is hydrogen, aralkyl, substituted aralkyl, heteroaralkyl, substituted heteroaralkyl, aralkenyl, substituted aralkenyl, heteroaralkenyl, substituted heteroaralkenyl, $R_3R_4NC(O)(CH_2)x$-, $R_3S(O)_p$- or $R_3R_4NS(O)_p$-;

R_3 is hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aralkyl, substituted aralkyl, heteroaralkyl, substituted heteroaralkyl, aralkenyl, substituted aralkenyl, heteroaralkenyl or substituted heteroaralkenyl, or R_1 and R_3 taken together with the -N-$S(O)_p$- moiety or the -N-$S(O)_p$-NR_4- moiety through which R_1 and R_3 are linked form a 5 to 7 membered heterocyclyl or substituted heterocyclyl; and

R_4 is hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aralkyl, substituted aralkyl, heteroaralkyl or substituted heteroaralkyl, or R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a 4 to 7 membered heterocyclyl or substituted heterocyclyl;

X_1 and X_{1a} are independently selected from H, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, substituted heteroaralkyl, or X_1 and X_{1a} taken together form oxo;

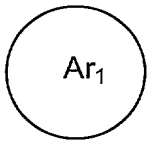
X_2 and X_{2a} taken together form oxo;

X_3 is H, hydroxy, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted

heteroaryl, aralkyl, substituted aralkyl, heteroaralkyl or substituted heteroaralkyl, or X_3 and one of X_1 and X_{1a} taken together form a 4 to 7 membered cycloalkyl;

X_4 is H, alkyl, substituted alkyl, aralkyl or substituted aralkyl;

X_5, X_{5a} and X_{5b} are independently selected from H, R_5R_6N-, (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-, R_7O-, R_5R_6NCO-, $R_5R_6NSO_2$-, R_7CO-, halo, cyano, nitro and $R_8(O)CCH_2$-, and one of X_5, X_{5a} and X_{5b} is a substituent that is alpha to a nitrogen of the ring of



that is distal to Z and is selected from the group consisting of H, hydroxy, H_2N-, (lower alkyl and substituted lower alkyl)HN-, (hydroxy)HN-, (alkoxy)HN- and (amino)HN-;

Y^1 and Y^2 are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aralkyl, substituted aralkyl, heteroaralkyl or substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 membered heterocyclyl;

R_5 and R_6 are independently H, lower alkyl or substituted lower alkyl, or one of R_5 and R_6 is H and the other of R_5 and R_6 is $R_8(O)CCH_2$- or lower acyl;

R_7 is H, lower alkyl, substituted lower alkyl, lower acyl or $R_8(O)CCH_2$- ;

R_8 is H, optionally substituted lower alkyl, alkoxy or hydroxy;

m is 1; p and r are independently 1 or 2; s is 0, 1 or 2; and x is 1, 2, 3, 4, or 5, or

a pharmaceutically acceptable salt, N-oxide, hydrate or solvate thereof.

2. (Amended) The compound of claim 1, wherein:

Z is alkylenyl;

R_1 is hydrogen, alkyl, substituted alkyl, aralkyl, substituted aralkyl, heteroaralkyl, substituted heteroaralkyl, $R'O(CH_2)_X$-, $R'O_2C(CH_2)_X$-, $Y^1Y^2NC(O)(CH_2)_X$-, or $Y^1Y^2N(CH_2)_X$-;

R' is hydrogen, alkyl, substituted alkyl, aralkyl, substituted aralkyl, heteroaralkyl, or substituted heteroaralkyl;

R_2 is $R_3S(O)_p$- or $R_3R_4NS(O)_p$-;

R_3 is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aralkyl, substituted aralkyl, heteroaralkyl, substituted heteroaralkyl, aralkenyl, substituted aralkenyl, heteroaralkenyl or substituted heteroaralkenyl, or R_1 and R_3 taken together with the -N-S(O)$_p$- moiety or the -N-S(O)$_p$-NR_4- moiety through which R_1 and R_3 are linked form a 5 to 7 membered heterocyclyl or substituted heterocyclyl;

R_4 is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aralkyl, substituted aralkyl, heteroaralkyl or substituted heteroaralkyl, or R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a 4 to 7 membered heterocyclyl or substituted heterocyclyl; and

Y^1 and Y^2 are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroaralkyl or optionally substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 membered heterocyclyl; or

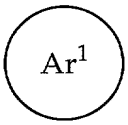
a pharmaceutically acceptable salt, N-oxide, hydrate or solvate thereof.

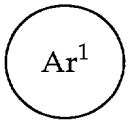
8. (Amended) The compound of claim 1 wherein R_1 is H, heteroaralkyl, substituted heteroaralkyl, aralkyl, substituted aralkyl, alkyl or substituted alkyl.

11. (Amended) The compound of claim 9 wherein R_3 is phenyl, substituted phenyl, naphthyl, substituted naphthyl, thienyl, substituted thienyl, benzothienyl, substituted benzothienyl, thienyopyridyl, substituted thienyopyridyl, quinolinyl, substituted quinolinyl, isoquinolinyl or optionally substituted isoquinolinyl.

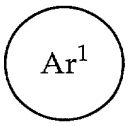
12. (Amended) The compound of claim 1 wherein Z is methylenyl.

22. (Amended) The compound of claim 1, wherein Z is bonded to said moiety through the 5 membered ring.

23. (Amended) The compound of claim 1 wherein one of X_5, X_{5a} and X_{5b} is a substituent that is on the 

ring proximal to Z, at a position that is alpha to where Z is attached to 

and is selected from the group consisting of H, hydroxy and amino.

25. (Amended) The compound of claim 1 wherein said one of X_5, X_{5a} and X_{5b} that substitutes the ring of 

distal to Z at the position alpha to a nitrogen thereof is H or (H, lower alkyl, substituted lower alkyl, hydroxy or amino)HN-.

26. (Amended) A compound according to claim 1 which is selected from

1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)amino] pyrrolidin-2-one;

2-(5-Chlorothiophen-2-yl)ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-yl-methyl)pyrrol-idin-3-(R)-yl]amide;

{[2-(5-Chlorothiophen-2-yl)ethenesulfonyl]-[2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-yl-methyl)pyrrol-idin-3-(R)-yl]amino}acetic acid isopropyl ester;

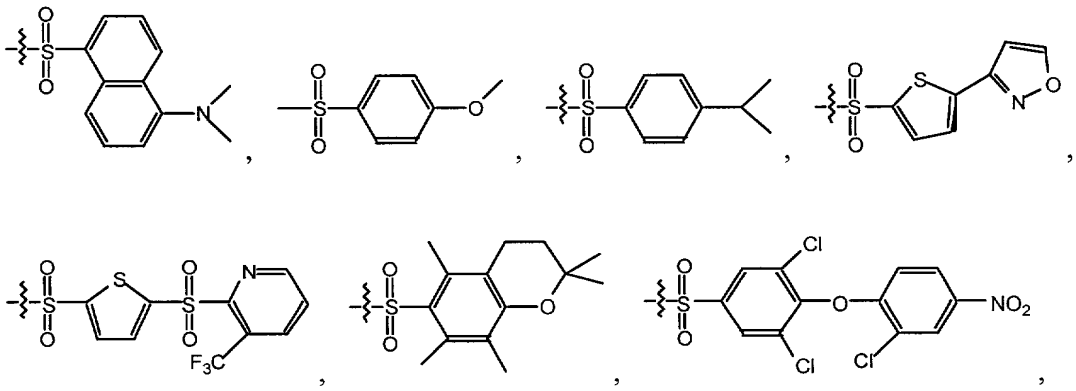
5'Chloro-[2,2']bithiophenyl-5-sulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-yl-methyl)-pyrrol-idin-3(S)-yl]-amide;

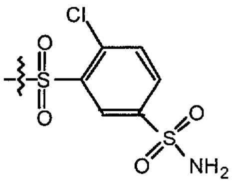
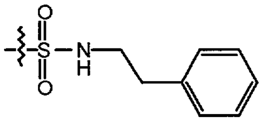
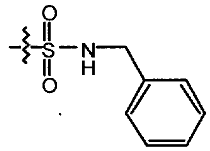
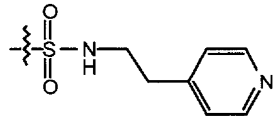
2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-yl-methyl)-pyrrolidin-3-(S)-yl]-amide; and

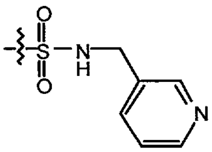
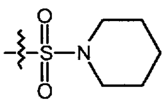
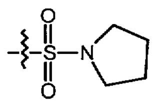
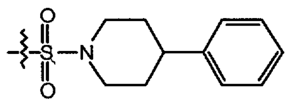
2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-yl-methyl)-pyrrolidin-3-(S)-yl]-amide.

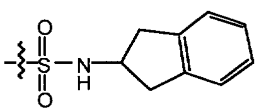
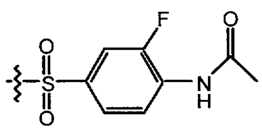
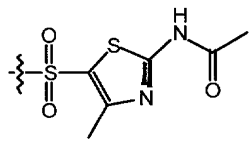
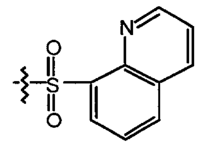
27. (Amended) A compound according to claim 1 which is selected from 2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-yl-methyl)-pyrrolidin-3-(S)-yl]-amide and thieno[3,2-b]pyridine-2-sulfonic acid [2-oxo-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide ditrifluoroacetate.

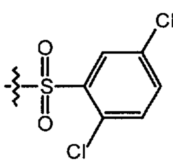
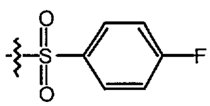
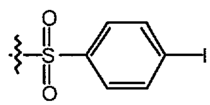
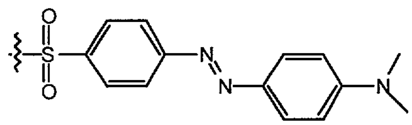
28. (Amended) A compound according to claim 1 wherein X_1, X_{1a}, X_3 and X_4 are H; and R_2 is a radical selected from the group consisting of

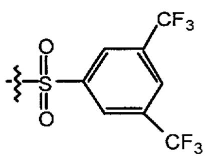
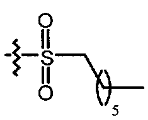
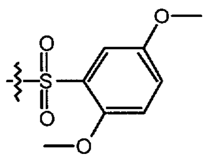
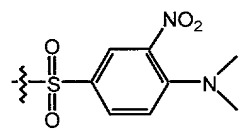


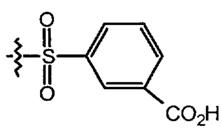
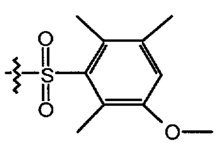
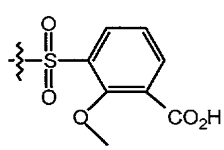
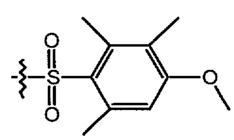
 ,  ,  ,  ,

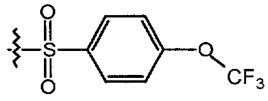
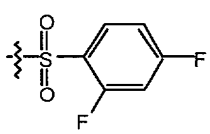
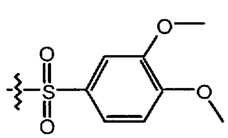
 ,  ,  ,  ,

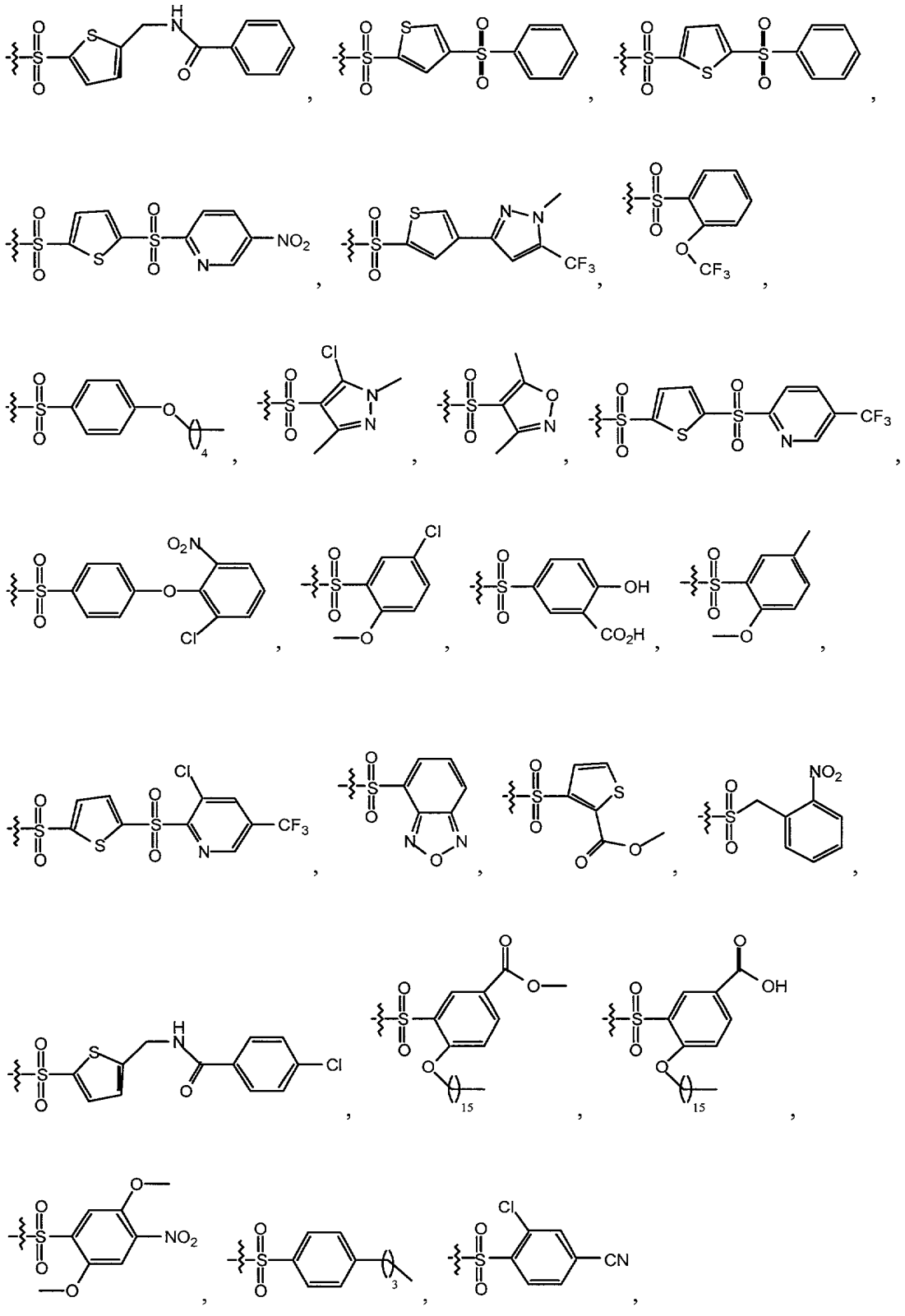
 ,  ,  ,  ,

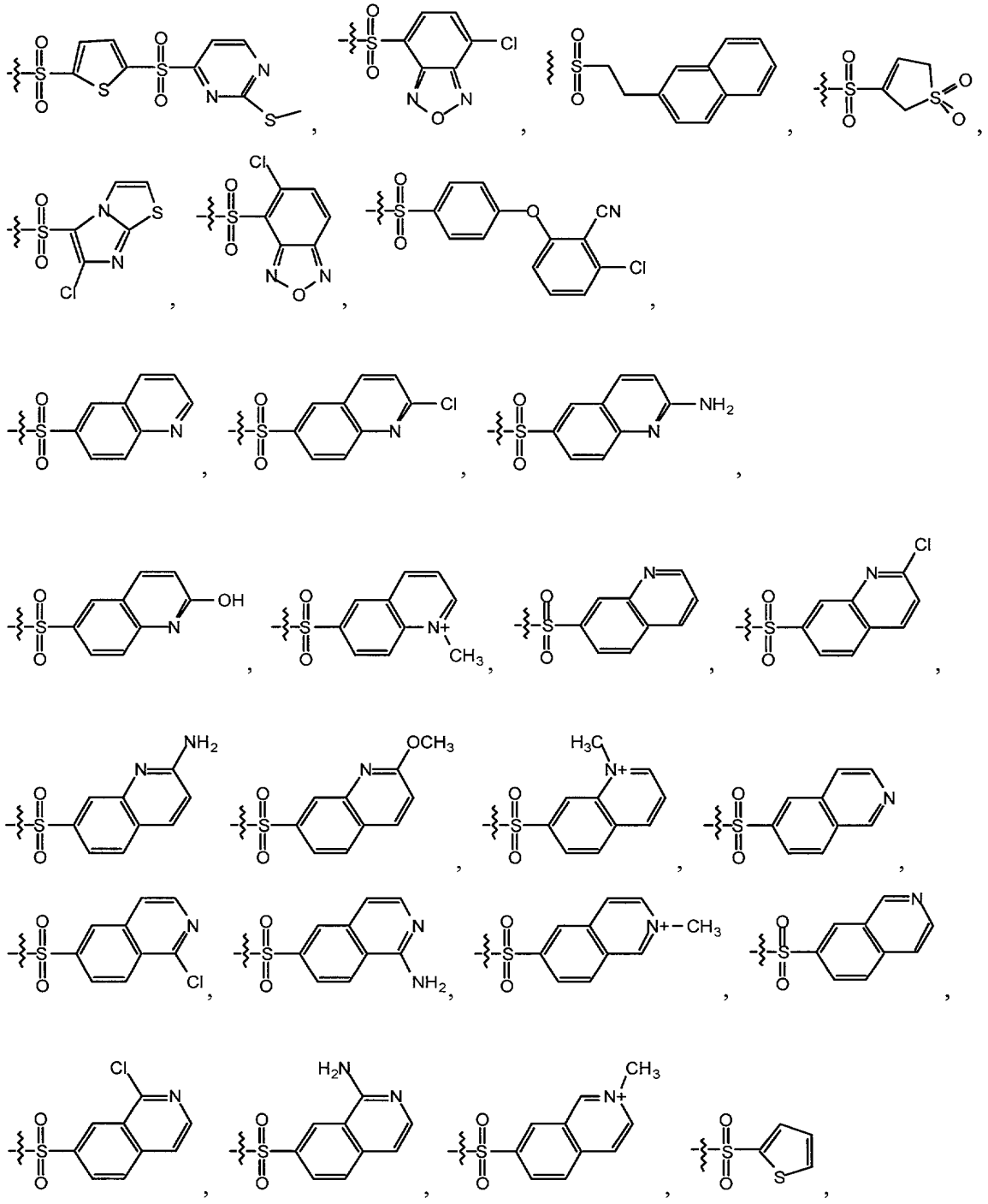
 ,  ,  ,  ,

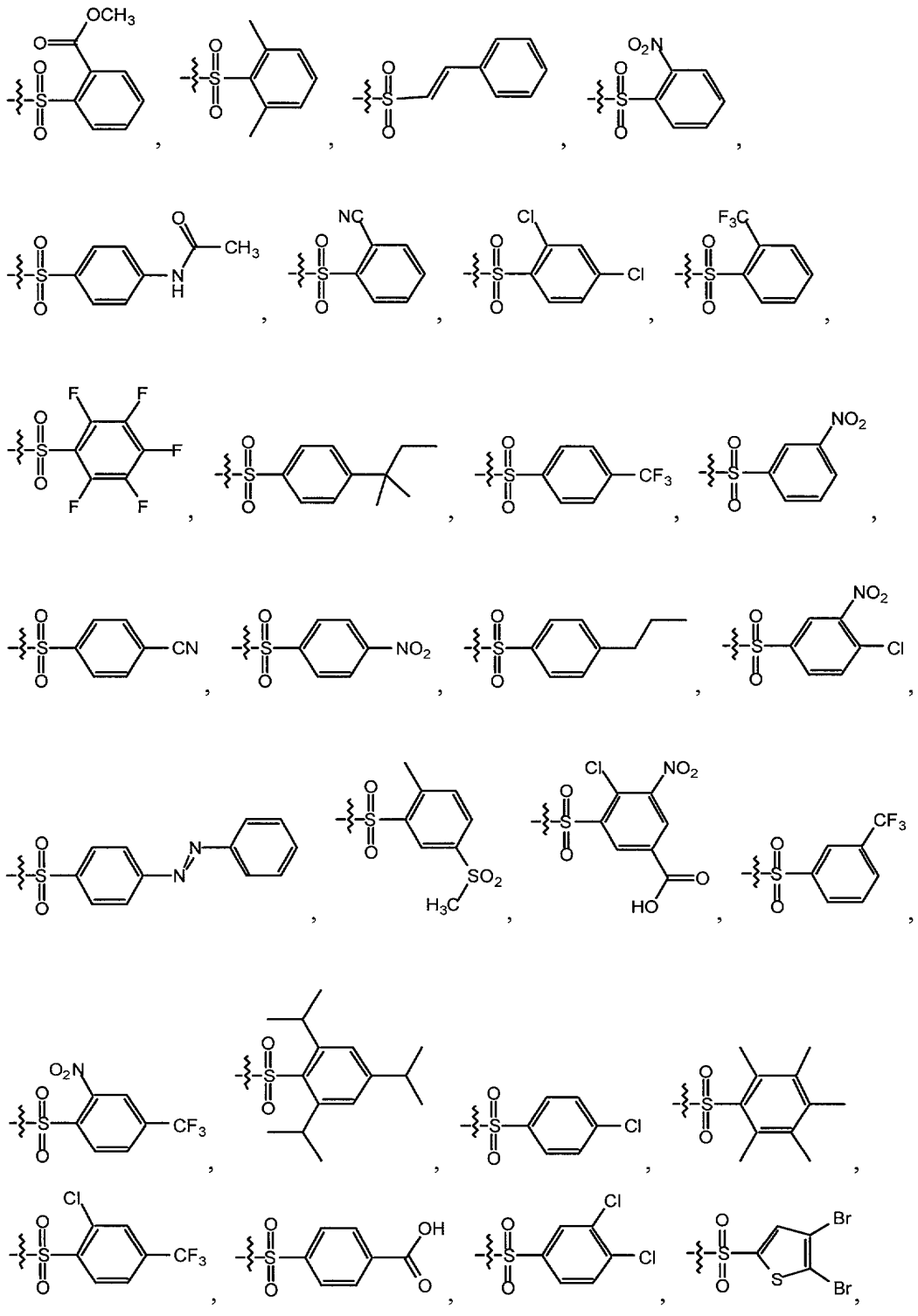
 ,  ,  ,  ,

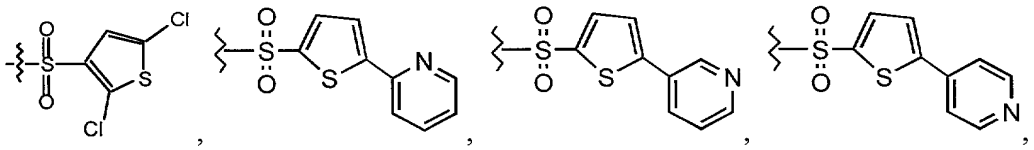
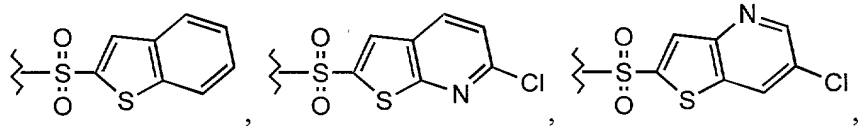
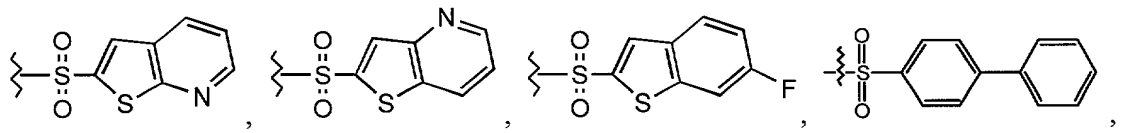
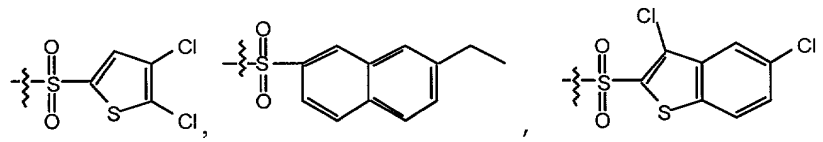
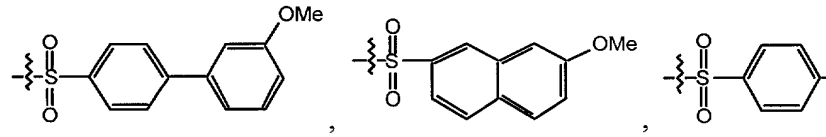
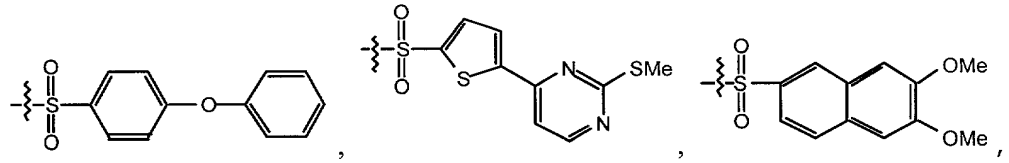
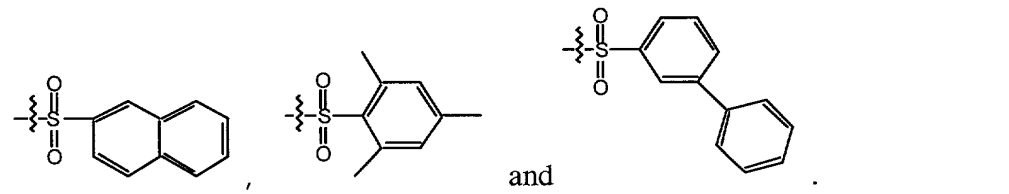
 ,  ,  ,  ,

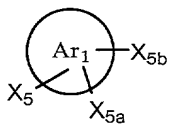
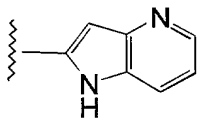
 ,  ,  ,

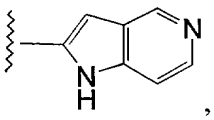
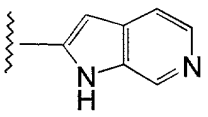
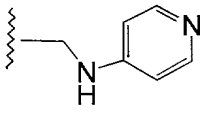


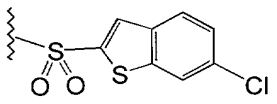
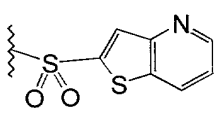
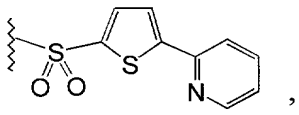











and

29. (Amended) A compound according to claim 1 wherein R_1, X_1, X_{1a}, X_3 and X_4 are H;  is selected from the group consisting of  ,


, 
and 
; and R_2 is a radical selected from the group consisting of:


, 
, 
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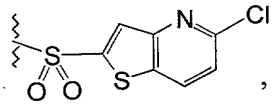
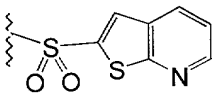
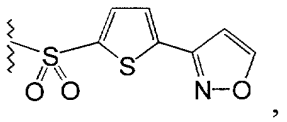

, 
, 
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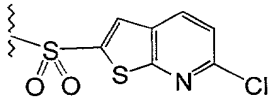
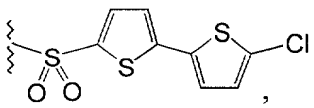
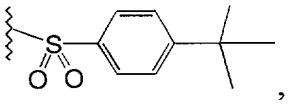

, 
, 
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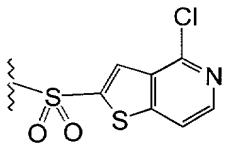
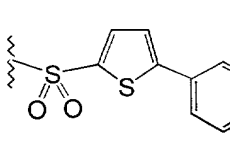
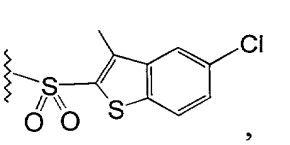

, 
, 
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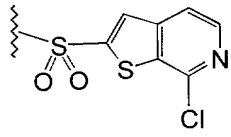
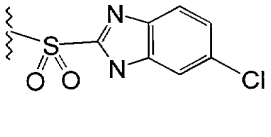

and 
;

REMARKS

This amendment is submitted prior to examination of the above-identified Divisional Patent Application. The specification has been amended to insert a priority claim to U.S. Patent Application Serial No. 09/453,307 filed December 12, 1999, which is a continuation-in-

part of International Application No. PCT/US99/12312, filed June 3, 1999, which application is a continuation-in-part of U.S. Patent Application Serial No. 09/090,492 filed June 3, 1998, which application, in turn, is a continuation-in-part of International Application No. PCT/US97/22406 filed December 3, 1997, which, in turn, claims priority benefit of U.S. Provisional Application No. 60/033,159, filed December 13, 1996. Claims 3-5, 7, 13, 15 to 21 and 42 have been canceled and claims 1, 2, 8, 11, 12, 22, 23 and 25-29 have amended to limit the claims to subject matter restricted from the parent application, i.e., Claim Group I.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned " **Version with markings to show changes made**." A favorable first action on the merits is respectfully requested. The Examiner is requested to telephone the undersigned if there are any issues requiring resolution.

Finally, the Examiner is authorized to charge Applicant's Deposit Account No. 18-1982 for any charges in connection with this Preliminary Amendment.

Respectfully submitted,

Dated: July 30, 2001

Peter J. Butch III
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The paragraph beginning at line 5 of page 1 has been amended as follows:

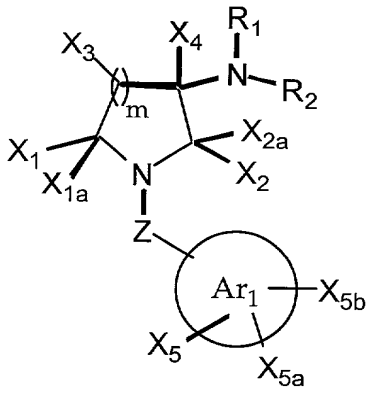
This application is a divisional of U.S. Application No. 09/453,307, filed December 12, 1999, which is a continuation-in-part of International Application No. PCT/US99/12312, filed June 3, 1999, which is, in turn, a continuation-in-part of U.S. Application No. 09/090,492, filed June 3, 1998, which is, in turn, a continuation-in-part of International Application No. PCT/US97/22406, filed December 3, 1997, which ~~is~~, in turn, claims priority benefit ~~a continuation-in-part~~ of U.S. Provisional Application No. 60/033,159, filed December 13, 1996, ~~now abandoned~~ the disclosures of all of which are incorporated herein by reference.

In the claims:

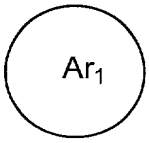
Claims 3-5, 7, 13, 15 to 21 and 42 have been cancelled, without prejudice.

Claims 1, 2, 8, 11, 12, 22, 23 and 25-29 have been amended as follows:

1. (Amended) A compound of formula I

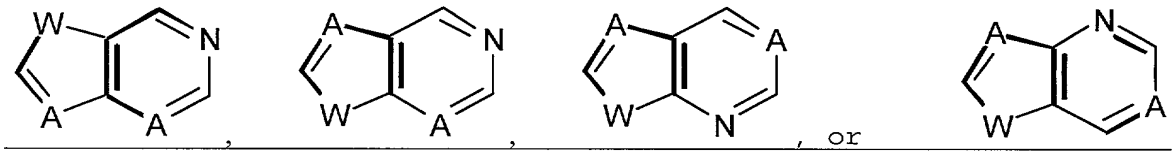


(I)

wherein 

is ~~a monocyclic heteroaryl group containing at least one nitrogen atom, or a bicyclic heteroaryl group which includes a first proximal ring that is attached to~~

~~Z and a ring distal to said first ring, said distal ring including at least one nitrogen atom~~ an optionally substituted moiety of formula



, , , or

in which W is NR_{11}, wherein R_{11} is H, alkyl, aralkyl, heteroaralkyl or $R_8(O)CCH_2$-, and A is CH;

Z is alkylenyl, $-(CH_2)_rC(O)NR"(CH_2)_s-$, $-(CH_2)_sR"NC(O)(CH_2)_r-$, ~~$-(CH_2)_rNR"(CH_2)_s-$~~ or $-(CH_2)_sNR"(CH_2)_r-$;

R_1 is hydrogen, alkyl, ~~optionally~~ substituted alkyl, alkenyl, ~~optionally~~ substituted alkenyl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl, ~~optionally~~ substituted heteroaralkyl, $R'O(CH_2)_X$-, $R'O_2C(CH_2)_X$-, $R'C(O)(CH_2)_X$-, $Y^1Y^2NC(O)(CH_2)_X$- or $Y^1Y^2N(CH_2)_X$-;

R' and R" are independently hydrogen, alkyl, ~~optionally~~ substituted alkyl, aryl, ~~optionally~~ substituted aryl, heteroaryl, ~~optionally~~ substituted heteroaryl, aralkenyl, ~~optionally~~ substituted aralkenyl, heteroaralkenyl, ~~optionally~~ substituted heteroaralkenyl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl or ~~optionally~~ substituted heteroaralkyl;

R_2 is hydrogen, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl, ~~optionally~~ substituted heteroaralkyl, aralkenyl, ~~optionally~~ substituted aralkenyl, heteroaralkenyl, ~~optionally~~ substituted heteroaralkenyl, $R_3R_4NC(O)(CH_2)x$-, $R_3S(O)_p$- or $R_3R_4NS(O)_p$-;

R_3 is hydrogen, alkyl, ~~optionally~~ substituted alkyl, cycloalkyl, ~~optionally~~ substituted cycloalkyl, heterocyclyl, ~~optionally~~ substituted heterocyclyl, aryl, ~~optionally~~ substituted aryl, heteroaryl, ~~optionally~~ substituted heteroaryl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl, ~~optionally~~ substituted heteroaralkyl, aralkenyl, ~~optionally~~ substituted aralkenyl, heteroaralkenyl or ~~optionally~~ substituted heteroaralkenyl, or R_1 and R_3 taken

together with the -N-S(O)$_p$- moiety or the -N-S(O)$_p$-NR$_4$- moiety through which R$_1$ and R$_3$ are linked form a 5 to 7 membered heterocyclyl or ~~optionally~~ substituted heterocyclyl; ~~and~~

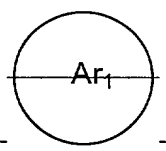
R_4 is hydrogen, alkyl, ~~optionally~~ substituted alkyl, cycloalkyl, ~~optionally~~ substituted cycloalkyl, aryl, ~~or optionally~~ substituted aryl, heteroaryl, ~~optionally~~ substituted heteroaryl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl or ~~optionally~~ substituted heteroaralkyl, or R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a ~~an optionally substituted~~ 4 to 7 membered heterocyclyl or substituted heterocyclyl;

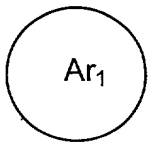
X_1 and X_{1a} are independently selected from H, alkyl, ~~optionally~~ substituted alkyl, aryl, ~~optionally~~ substituted aryl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaryl, ~~optionally~~ substituted heteroaryl, heteroaralkyl, ~~optionally~~ substituted heteroaralkyl, or X_1 and X_{1a} taken together form oxo;

X_2 and X_{2a} ~~are H, or~~ taken together form oxo;

X_3 is H, hydroxy, alkyl, ~~optionally~~ substituted alkyl, aryl, ~~optionally~~ substituted aryl, heteroaryl, ~~optionally~~ substituted heteroaryl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl or ~~optionally~~ substituted heteroaralkyl, or X_3 and one of X_1 and X_{1a} taken together form a 4 to 7 membered cycloalkyl;

X_4 is H, alkyl, ~~optionally~~ substituted alkyl, aralkyl, ~~optionally~~ or substituted aralkyl~~, or hydroxyalkyl~~;

X_5, X_{5a} and X_{5b} are independently selected from H, R_5R_6N-, (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-, R_7O-, R_5R_6NCO-, $R_5R_6NSO_2$-, R_7CO-, halo, cyano, nitro and $R_8(O)C(CH_2)_q$-, and ~~when~~  ~~is a bicyclic heteroaryl group,~~ one of X_5, X_{5a} and

X_{5b} is a substituent that is alpha to a nitrogen of the ~~said distal~~ ring of 

that is distal to Z and is selected from the group consisting of H, hydroxy and H_2N-, (lower alkyl and ~~optionally~~ substituted lower alkyl)HN (hydroxy)HN-, (alkoxy)HN-~~, or~~ and (amino)HN-;

Y^1 and Y^2 are independently hydrogen, alkyl, ~~optionally~~ substituted alkyl, aryl, ~~optionally~~ substituted aryl, heteroaryl, ~~optionally~~ substituted heteroaryl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl or ~~optionally~~ substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 membered heterocyclyl;

R_5 and R_6 are independently H, lower alkyl or ~~optionally~~ substituted lower alkyl, or one of R_5 and R_6 is H and the other of R_5 and R_6 is $R_8(O)CCH_2$- or lower acyl;

R_7 is H, lower alkyl, ~~optionally~~ substituted lower alkyl, lower acyl or $R_8(O)CCH_2$- ;

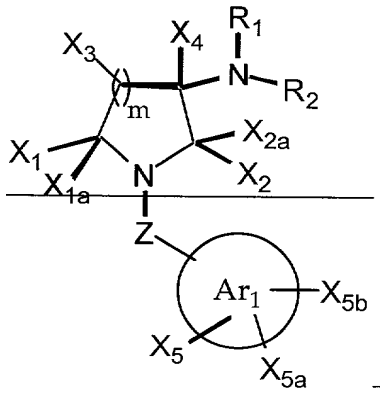
R_8 is H, lower alkyl, ~~optionally~~ substituted lower alkyl, alkoxy or hydroxy;

m is ~~0,~~ 1~~, 2 or 3~~; p and r are independently 1 or 2; ~~q is 0 or 1,~~ s is 0, 1 or 2; and

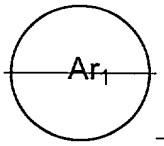
x is 1, 2, 3, 4, or 5, or

a pharmaceutically acceptable salt ~~thereof~~, ~~an~~ N-oxide ~~thereof~~, ~~a~~ hydrate ~~thereof~~ or ~~a~~ solvate thereof.

2. (Amended) The ~~A~~ compound of claim 1, ~~formula I~~



~~(I)~~ wherein



~~is a bicyclic heteroaryl which includes a first proximal ring that is attached to Z and a ring distal to said first ring, said distal ring including at least one nitrogen atom;~~

Z is alkylenyl;

R_1 is hydrogen, alkyl, ~~optionally~~ substituted alkyl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl, ~~optionally~~ substituted heteroaralkyl, $R'O(CH_2)_{x-}$, $R'O_2C(CH_2)_{x-}$, $Y^1Y^2NC(O)(CH_2)_{x-}$, or $Y^1Y^2N(CH_2)_{x-}$;

R' is hydrogen, alkyl, ~~optionally~~ substituted alkyl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl or ~~optionally~~ substituted heteroaralkyl;

R_2 is $R_3S(O)_{p-}$ or $R_3R_4NS(O)_{p-}$;

R_3 is alkyl, ~~optionally~~ substituted alkyl, cycloalkyl, ~~optionally~~ substituted cycloalkyl, heterocyclyl, ~~optionally~~ substituted heterocyclyl, aryl, ~~optionally~~ substituted aryl, heteroaryl, ~~optionally~~ substituted heteroaryl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl, ~~optionally~~ substituted heteroaralkyl, aralkenyl, ~~optionally~~ substituted aralkenyl, heteroaralkenyl or ~~optionally~~ substituted heteroaralkenyl, or R_1 and R_3 taken together with the -N-$S(O)_{p-}$ moiety or the -N-$S(O)_{p-}NR_4$- moiety through which R_1 and R_3 are linked form a 5 to 7 membered heterocyclyl or ~~optionally~~ substituted heterocyclyl; ~~and~~

R_4 is alkyl, ~~optionally~~ substituted alkyl, cycloalkyl, ~~optionally~~ substituted cycloalkyl, aryl, ~~or optionally~~ substituted aryl, heteroaryl, ~~optionally~~ substituted heteroaryl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl or ~~optionally~~ substituted heteroaralkyl, or R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a ~~an optionally substituted~~ 4 to 7 membered heterocyclyl or substituted heterocyclyl;

Y^1 and Y^2 are independently hydrogen, alkyl, ~~optionally~~ substituted alkyl, aryl, ~~optionally~~ substituted aryl, aralkyl, ~~optionally~~ substituted aralkyl, heteroaralkyl or ~~optionally~~ substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 membered heterocyclyl;

a pharmaceutically acceptable salt ~~thereof~~, ~~an~~ N-oxide ~~thereof~~, ~~a~~ hydrate ~~thereof~~ or ~~a~~ solvate thereof.

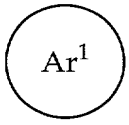
8. (Amended) The compound of claim 1 wherein R_1 is H, heteroaralkyl, ~~optionally~~ substituted heteroaralkyl, aralkyl, ~~optionally~~ substituted aralkyl, alkyl or ~~optionally~~ substituted alkyl.

11. (Amended) The compound of claim 9 wherein R_3 is phenyl, ~~optionally~~ substituted phenyl, naphthyl, ~~optionally~~ substituted naphthyl, thienyl, ~~optionally~~ substituted thienyl, benzothienyl, ~~optionally~~ substituted benzothienyl, thienopyridyl, ~~optionally~~ substituted thienyopyridyl, quinolinyl, ~~optionally~~ substituted quinolinyl, isoquinolinyl or ~~optionally~~ substituted isoquinolinyl.

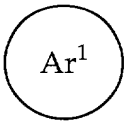
12. (Amended) The compound of claim 1 wherein Z is methylenyl ~~and m is 1~~.

22. (Amended) The compound of claim ~~21~~ 1, wherein Z is bonded to said moiety through the 5 membered ring.

23. (Amended) The compound of claim 1 wherein one of X_5, X_{5a} and X_{5b} is a substituent that is on the ~~proximal ring of bicyclic~~ 

ring proximal to Z, at a position that is alpha to where Z is attached to 

and is selected from the group consisting of H, hydroxy and amino.

25. (Amended) The compound of claim 1 wherein one of X_5, X_{5a} and X_{5b} that substitutes the ~~distal~~ ring of 

distal to Z at the position alpha to a nitrogen thereof is H or (H, lower alkyl, ~~optionally~~ substituted lower alkyl ~~loweralkyl~~, hydroxy or amino)HN-.

26. (Amended) A compound according to claim 1 which is selected from

~~3-[[1-(4-Aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]-(5-chloro-1H-indol-2-ylmethyl)amino]propionic acid methyl ester;~~

~~1-(4-Aminoquinolin-7-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)-(3-ethylbutyl)amino]pyrrolidin-2-one;~~

~~1-(4-Aminoquinolin-7-ylmethyl)-3-(R)-[benzyl-(5-chloro-1H-indol-2-ylmethyl)amino]pyrrolidin-2-one;~~

~~1-(4-Aminoquinolin-7-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)thiazol-5-ylmethylamino]pyrrolidin-2-one;~~

~~1-(4-Aminoquinolin-7-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)-(2H-pyrazol-3-ylmethyl))amino]pyrrolidin-2-one;~~

~~1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(6-chlorobenzo[b]thiophen-2-ylmethyl)amino]pyrrolidin-2-one;~~

~~1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(6-chlorothieno[2,3-b]pyridin-2-ylmethyl)amino]pyrrolidin-2-one;~~

1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)amino]pyrrolidin-2-one;

~~3-{[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-ylamino]methyl}-1H-quinolin-2-one;~~

~~1-(7-Aminothieno[3,2-b]pyridin-2-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)amino]pyrrolidin-2-one;~~

2-(5-Chlorothiophen-2-yl)ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)pyrrolidin-3-(R)-yl]amide;

{[2-(5-Chlorothiophen-2-yl)ethenesulfonyl]-[2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)pyrrolidin-3-(R)-yl]amino}acetic acid isopropyl ester;

~~1-(4-Aminoquinolin-7-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)amino]pyrrolidin-2-one;~~

~~5-Chloro-1H-benzoimidazole-2-sulfonic acid [1-(4-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]amide7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(R,S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide hydrochloride;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(R)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1-hydroxyisoquinolin-7ylmethyl)-2-oxopyrrolidin-3-(R,S)-yl] amide;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R,S)-yl] methylamide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methyl amide trifluoroacetate;~~

~~Benzo[b]thiophene-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1-amino-6-methoxyisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide hydrochloride;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(6-methoxyisoquinolin-7-ylmethyl)-2-oxo pyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~4-(2-Chloro-6-nitophenoxy)benzene sulfonic acid [1-(1-amino-6-methoxyisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1,6-diaminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(1,6-diaminoisoquinolin-7-yl-methyl)-2-oxo pyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)yl] amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(2-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~Benzo[b]thiophene-2-sulfonic acid [1-(2-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methyl amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(2-hydroxyquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methyl amide;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-5-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-5-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methyl amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(2-hydroxyquinolin-5-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methylamide;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-6-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(2-hydroxyquinolin-6-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(1H-benzimidazol-5-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [2-(1H-benzimidazol-5-ylethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(4-aminoquinazolin-6-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methylamide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(4-aminothieno[2,3-d]pyrimidin-6-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [2-(6-aminothieno[2,3-d]pyrimidin-6-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(7-aminothieno[2,3-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(7-hydroxythieno[2,3-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(4-aminothieno[3,2-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(R,S)-yl] amide trifluoroacetate;~~

~~7-Methoxynaphthalene-2-sulfonic acid [1-(4-hydroxythieno[3,2-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(R,S)-yl] amide trifluoroacetate;~~

~~Benzo[b]thiophene-2-sulfonic acid [1-(4-aminothieno[3,2-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(R,S)-yl] amide trifluoroacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;~~

~~Thieno[2,3-b]pyridine-2-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;~~

~~4-Pyridin-3-yl-thiophene-2-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;~~

5'Chloro-[2,2']bithiophenyl-5-sulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-pyrrolidin-3(S)-yl]-amide;

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide;

~~5' -Chloro-[2,2']bithiophenyl -5-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;~~

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-quinazolin-6-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-thieno[2,3-d]pyrimidin-6-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;~~

~~5' -Chloro-[2,2']bithiophenyl -5-2-sulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1,6-diamino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;~~

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;~~

~~5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;~~

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide;

~~3-(R)-5 Chlorothiophen-2-yl)-ethenesulphonic acid [1-(4-aminoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~2-(S)-[[1-(4-Amino-quinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-(6-chloro-benzo[b]thiophene-2-sulfonyl)-amino]-acetic acid methyl ester, trifluoroacetate;~~

~~2-(S)-6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-quinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide, trifluoroacetate;~~

~~2-(s)-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(4-amino-quinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide, trifluoroacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid [1-(4-amino-quinolin-6-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide, ditrifluoroacetate;~~

~~N-(3-Amino-pyridin-4-yl)-2-[3-(7-methoxy-naphthalene-2-sulfonylamino)-2-oxo-pyrrolidin-1-yl]-acetamide;~~

~~2-[3-(7-Methoxy-naphthalene-2-sulfonylamino)-2-oxo-pyrrolidin-1-yl]-N-pyridin-4-yl-acetamide;~~

~~6-Chlorobenzo[b]thiophene-2-sulfonic acid {2-oxo-1-[2-(pyridin-4-yl-amino)ethyl]-pyrrolidin-3-(S)-yl}-amide trifluoroacetate;~~

~~5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid {2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide;~~

~~6-Chloro-thieno[2,3-b]pyridine-2-sulfonic acid {2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide trifluoacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid {2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide ditrifluoroacetate;~~

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid {2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide;~~

~~(S)-5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid {1-[2-(2-amino-3-chloro-pyridin-4-ylamino)-ethyl]-2-oxo-pyrrolidin-3-yl}-amide ditrifluoroacetate;~~

~~(S)-6-Chloro-benzo[b]thiophene-2-sulfonic acid {1-[2-(2-amino-3-chloro-pyridin-4-ylamino)-ethyl]-2-oxo-pyrrolidin-3-yl}-amide ditrifluoroacetate;~~

~~((6-Chloro-benzo[b]thiophene-2-sulfonyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3(-yl}-amino)-acetic acid methyl ester;~~

~~((6-Chloro-benzo[b]thiophene-2-sulfonyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid allyl-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid methyl-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide;~~

~~(S)-2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid {1-[2-(2-amino-3-chloro-pyridin-4-ylamino)-ethyl]-2-oxo-pyrrolidin-3-yl}-amide trifluoroacetate;~~

~~(S)-Thieno[3,2-b]pyridine-2-sulfonic acid {1-[2-(2-amino-3-chloro-pyridin-4-ylamino)-ethyl]-2-oxo-pyrrolidin-3-yl}-amide ditrifluoroacetate;~~

~~([2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid methyl ester;~~

~~([2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid isopropyl ester;~~

~~([2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid trifluoroacetate;~~

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid (2-methoxy-ethyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide trifluoroacetate;~~

~~([2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid ethyl ester trifluoroacetate;~~

~~3-(5-Chloro-thiophen-2-yl)-N-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-acrylamide trifluoroacetate;~~

~~1-[1-(4-Aminoquinazolin-7ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-3-(4-chlorophenyl)urea trifluoroacetate;~~

~~N-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-2-(5-chlorothiophen-2-yloxy)acetamide trifluoroacetate;~~

~~1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-indol-2-ylmethyl)amino] pyrrolidin-2-one trifluoroacetate;~~

~~1-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-3-(5-chlorothiophen-2-yl) urea trifluoroacetate and 5-Chlorothiophene-2-carboxylic acid [1-(4-aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;~~

~~{[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-[3-(5-chlorothiophen-2-yl)acryloyl]amino}acetic acid methyl ester trifluoroacetate;~~

~~6-Chlorobenzo[b]thiophene-2-sulfonic acid [1-(4-aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate;~~

~~1-(4-Aminoquinolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-indol-2-ylmethyl)amino]pyrrolidin-2-one trifluoroacetate;~~

~~1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[3-(5-chlorothiophen-2-yl)allylamino]pyrrolidin-2-one trifluoroacetate;~~

~~N-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-3-(5-chlorothiophen-2-yl)acrylamide trifluoroacetate;~~

~~1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-benzimidazol-2-ylmethyl)amino]pyrrolidin-2-one trifluoroacetate;~~

~~{[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl][2-(5-chlorothiophen-2-yl)ethenesulfonyl]amino}acetic acid methyl ester trifluoroacetate;~~

~~{[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl](5-chloro-1H-indol-2-ylmethyl)amino]acetic acid methyl ester trifluoroacetate;~~

~~{[1-(Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl][3-(5-chlorothiophen-2-yl)allyl]amino}acetic acid methyl ester trifluoroacetate;~~

~~{1-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-3-(5-chlorothiophen-2-yl)ureido}acetic acid methyl ester trifluoroacetate;~~

~~N-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]-3-(5-chlorothiophen-2-yl)acrylamide trifluoroacetate;~~

~~1-(4-Aminoquinazolin-7-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)amino] pyrrolidin-2-one trifluoroacetate;~~

~~1-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]-3-(5-chlorothiophen-2-yl) urea trifluoroacetate and 5-Chlorothiophene-2-carboxylic acid [1-(4-aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate;~~

~~{[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl](5-chloro-1H-indol-2-ylmethyl)amino]acetic acid methyl ester trifluoroacetate;~~

~~1-(4-Aminoquinolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-benzimidazol-2-ylmethyl)amino]pyrrolidin-2-one trifluoroacetate;~~

~~5-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-quinazolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3(S)-yl]-amide;~~

~~7-Methoxy-naphthalene-2-sulfonic acid [1-(4-amino-quinazolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(4-amino-quinazolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-quinazolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

~~5-Chloro-benzo[b]thiophene-2-sulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~5-Chloro-benzo[b]thiophene-2-sulfonic acid [(S)-1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~5-Chloro-benzo[b]thiophene-2-sulfonic acid [(S)-1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid [(S)-1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid [(S)-1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [(S)-1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [(S)-1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide;~~

~~6-Chlorobenzo[b]thiophene-2-sulfonic acid [1-(4-aminoquinolin-7-yl methyl)-2-oxo-3(R)-pyrrolidin-3-yl]amide trifluoroacetate; and~~

~~2-(5-Chlorothiophen-2-yl)-ethenesulfonic acid [1-(4-aminoquinazolin-7-yl methyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate.~~

27. (Amended) A compound according to claim 1 which is selected from

~~7-Methoxynaphthalene-2-sulfonic acid[1-(6-methoxyisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

~~1-(4-Aminoquinolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-benzimidazol-2-ylmethyl)amino]pyrrolidin-2-one trifluoroacetate;~~

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide;

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(4-amino-quinazolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

~~2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;~~

~~Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate;~~

~~6-Chlorobenzo[b]thiophene-2-sulfonic acid {2-oxo-1-[2-(pyridin-4-yl-amino)ethyl]-pyrrolidin-3-(S)-yl}-amide trifluoroacetate;~~

~~((6-Chloro-benzo[b]thiophene-2-sulfonyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3(-yl}-amino)-acetic acid methyl ester;~~

Thieno[3,2-b]pyridine-2-sulfonic acid [2-oxo-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide ditrifluoroacetate;

~~Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

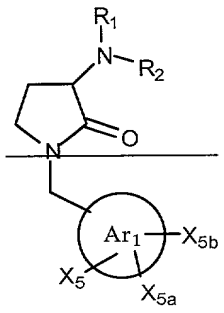
~~2(S)-(5Chloro-thiophen2-yl)-ethenesulfonic acid [1-(4amino-quinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;~~

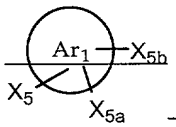
~~6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(1,6-diamino-isoquinolin-7yl methyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide bistrifluoroacetate;~~

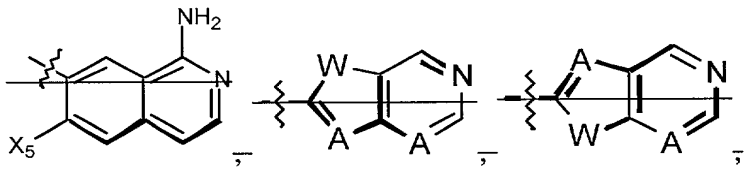
~~6-Chlorobenzo[b]thiophene-2-sulfonic acid [1-(4-aminoquinolin-7-yl methyl)-2-oxo-3(R)-pyrrolidin-3-yl]amide trifluoroacetate; and~~

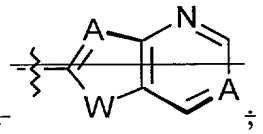
~~2-(5-Chlorothiophen-2-yl)-ethenesulfonic acid [1-(4-aminoquinazolin-7-yl methyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate.~~

28. (Amended) A compound according to claim 1 ~~of the formula~~

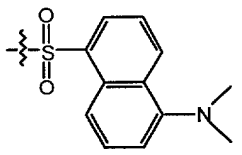
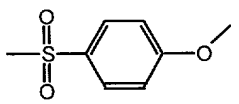
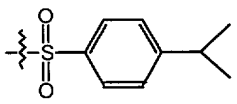
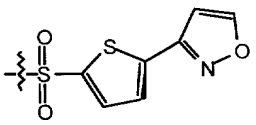


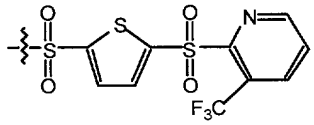
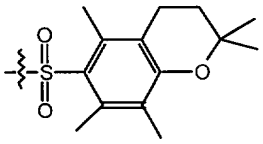
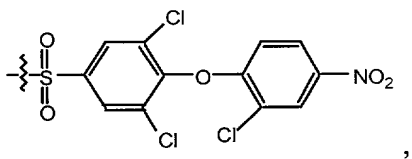
wherein X_1, X_{1a}, X_3 and X_4 are H;  ~~is a radical selected from the group consisting of~~

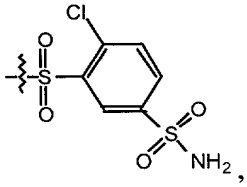
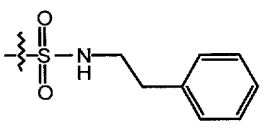
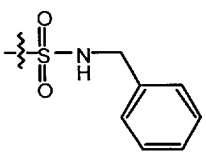
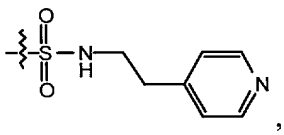


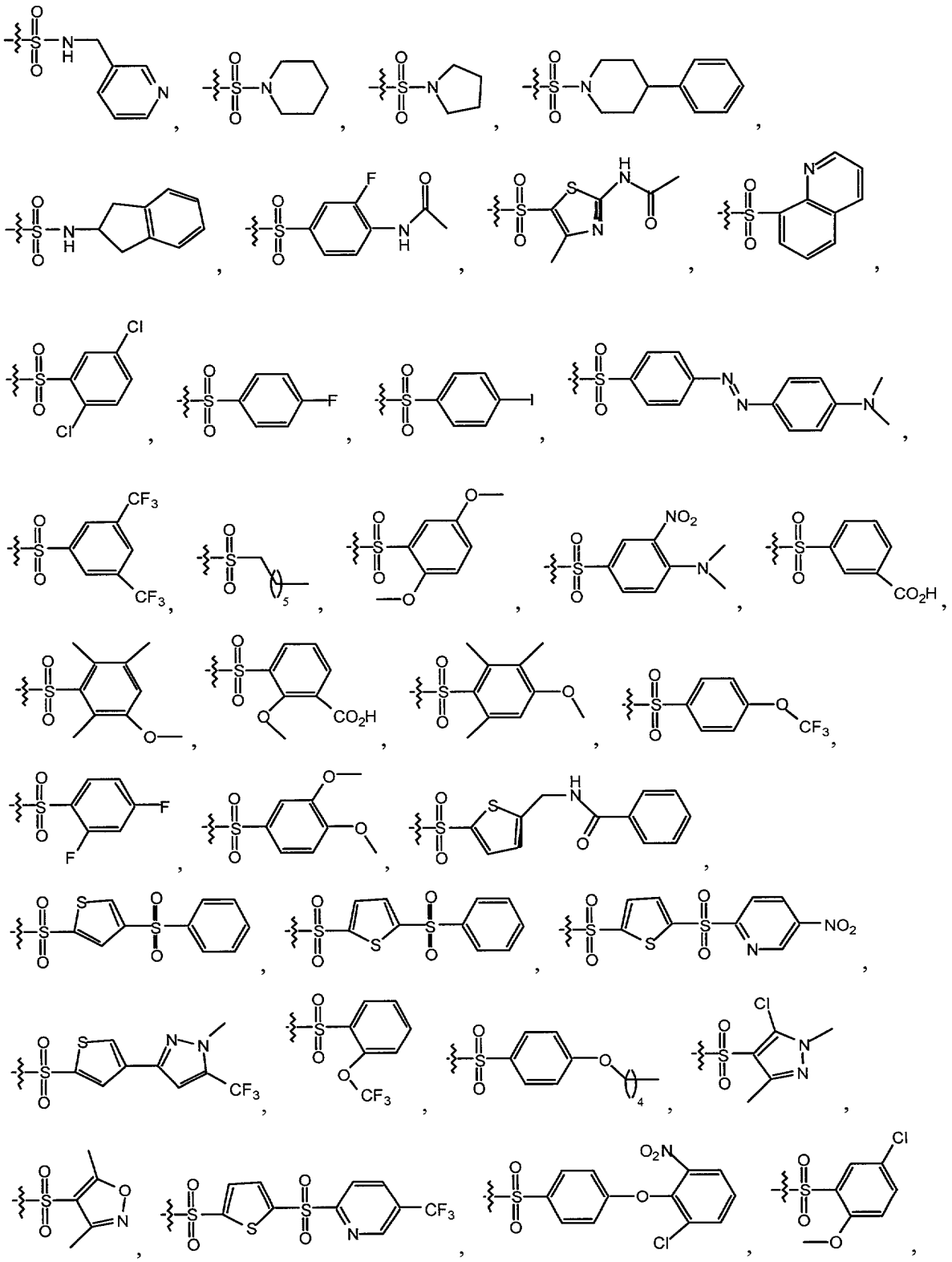
~~, and~~  ~~;~~

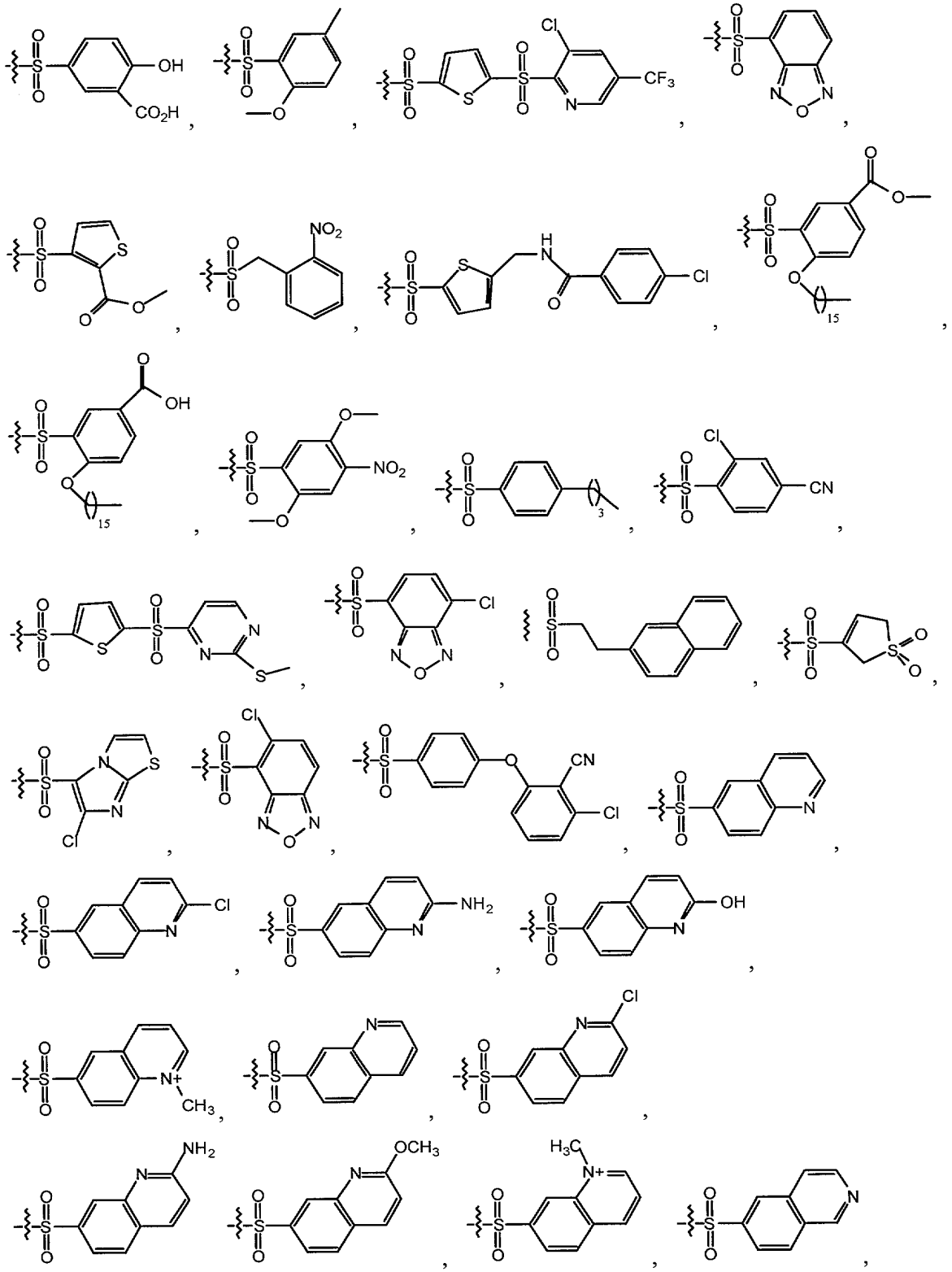
~~W is S, O or NR_{11}, wherein R_{11} is H, alkyl, aralkyl, heteroaralkyl or $R_8(O)C(CH_2)_q$-; A is CH or N;~~ and R_2 is a radical selected from the group consisting of

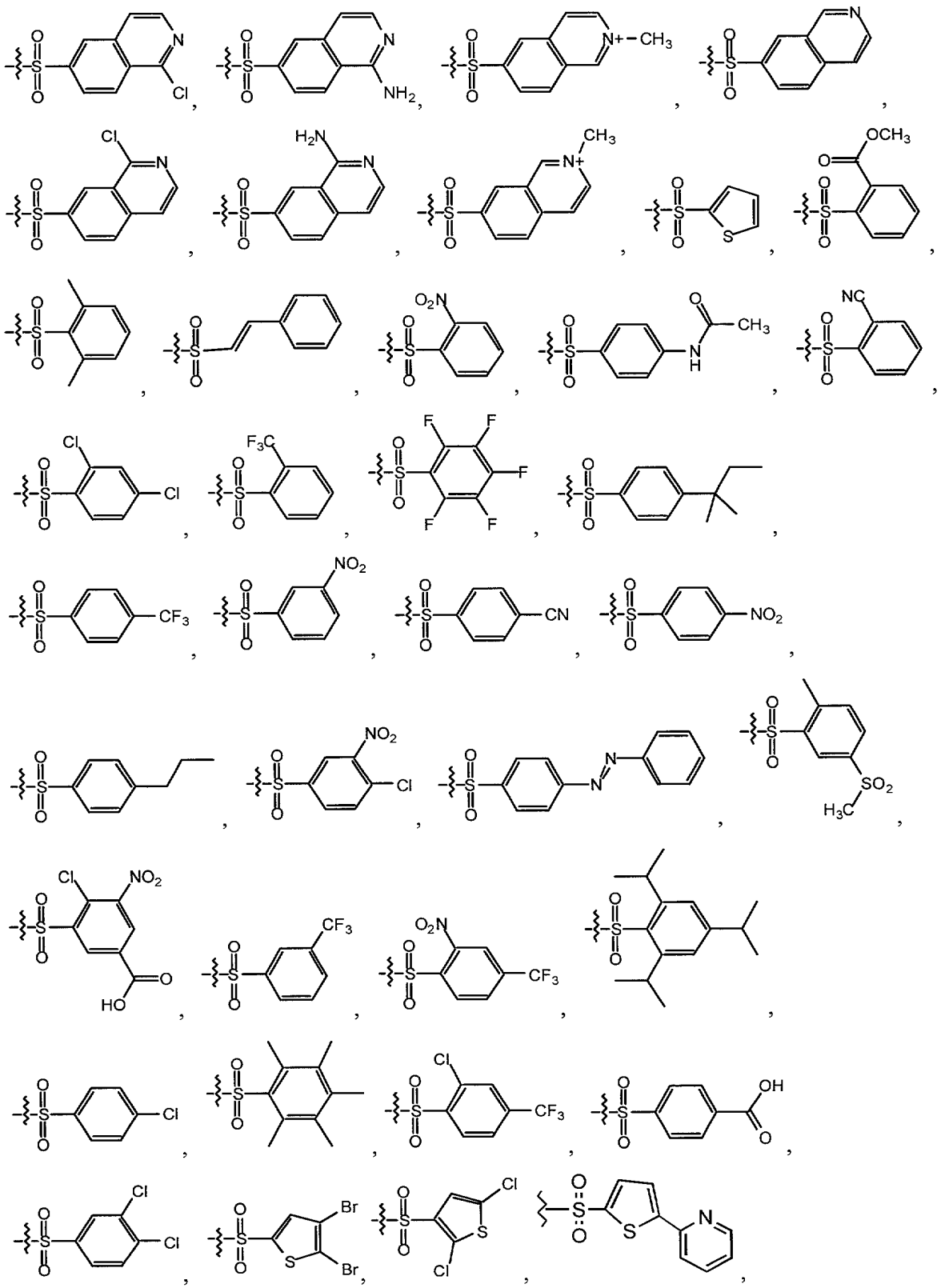
 ,  ,  ,  ,

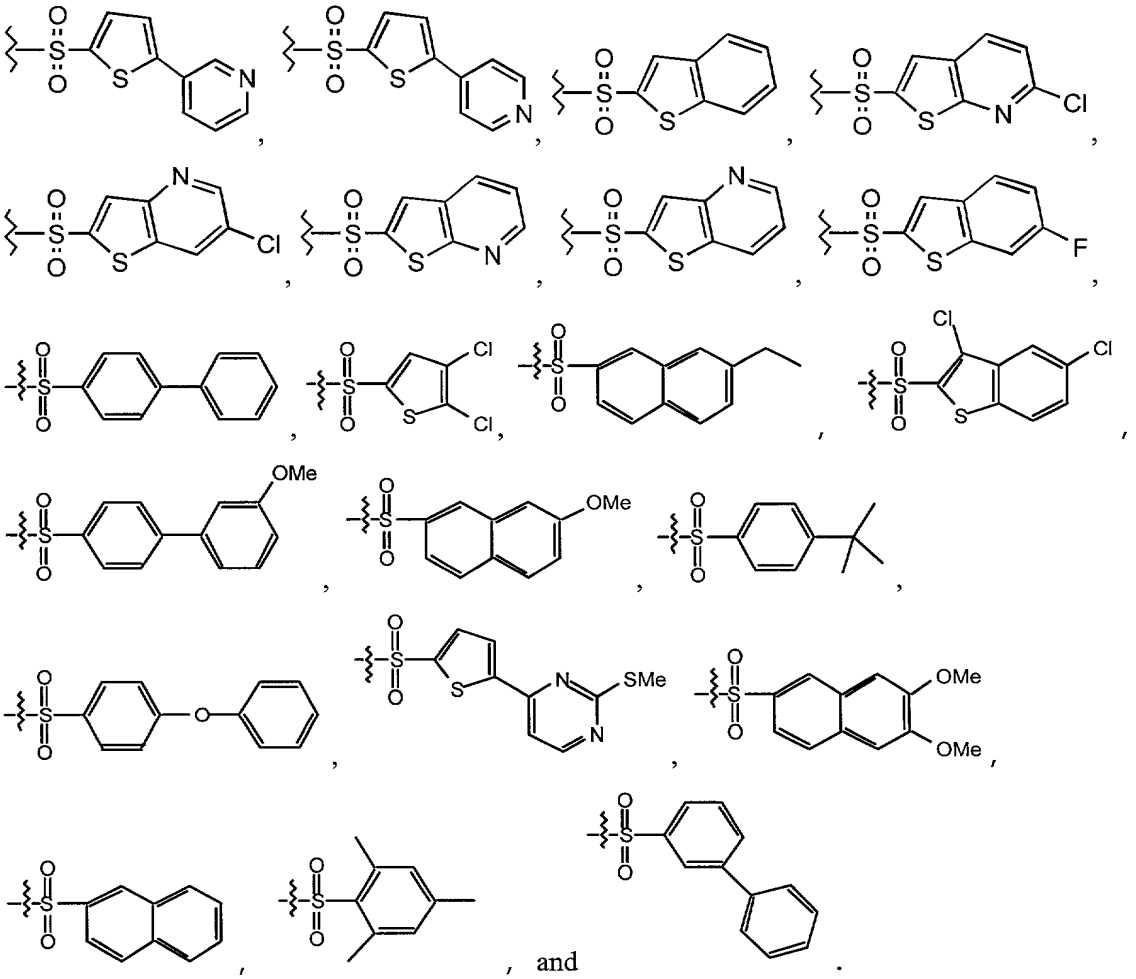
 ,  ,  ,

 ,  ,  , 

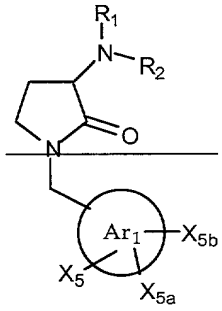


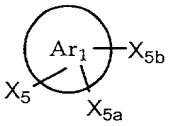


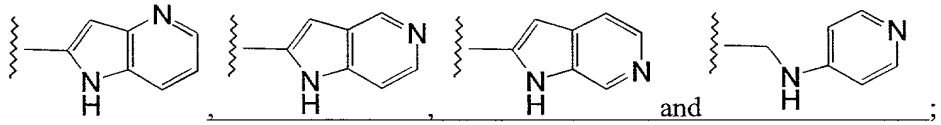




29. (Amended) A compound according to claim 1 ~~of the formula~~

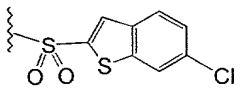
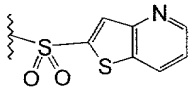
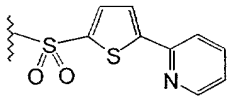
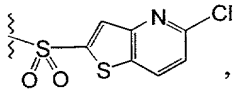
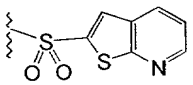
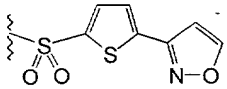
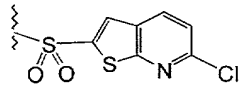
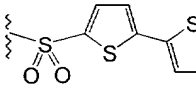
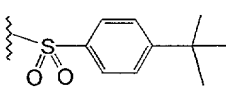
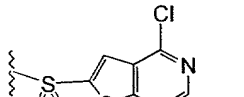
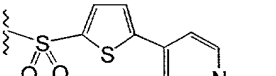
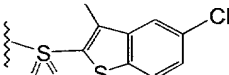
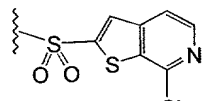
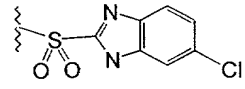


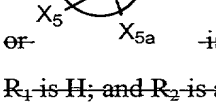
wherein R_1, X_1, X_{1a}, X_3 and X_4 are H;  is selected from the group consisting of



and ;

~~R_1 is H;~~ and R_2 is a radical selected from the group consisting of: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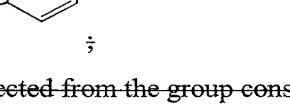
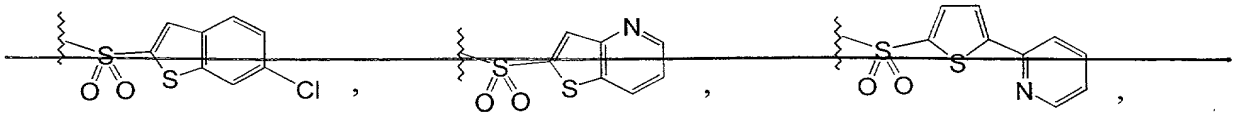


~~,~~ ~~.~~

~~or~~ ~~is~~

~~;~~

~~R_1 is H; and R_2 is a radical selected from the group consisting of:~~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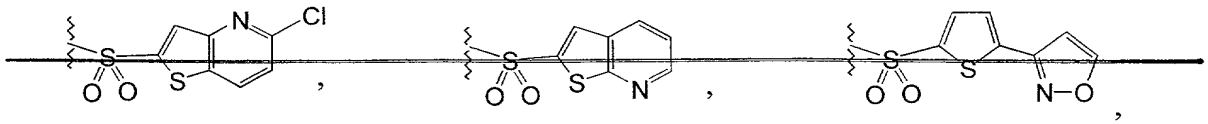
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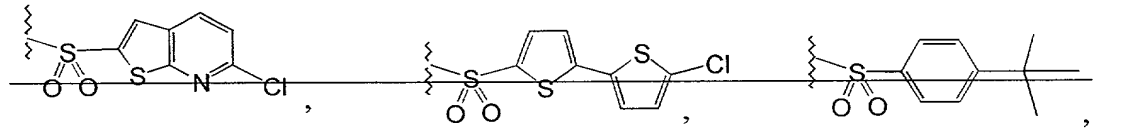
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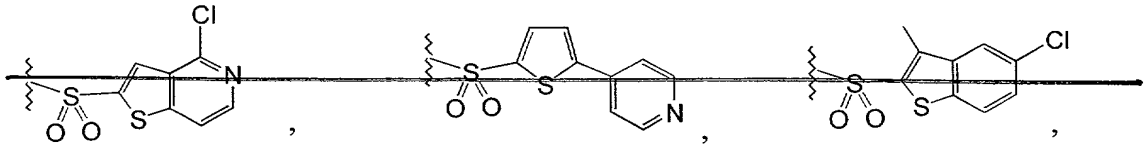
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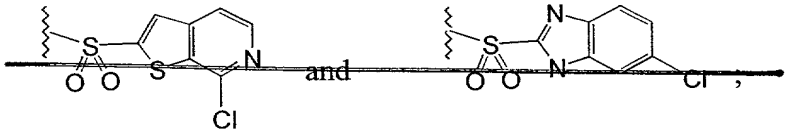
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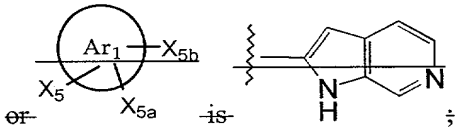
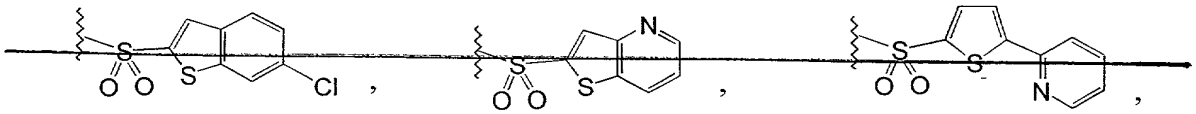

or ~~is~~ ;

~~R_1 is H; and R_2 a radical selected from the group consisting of:~~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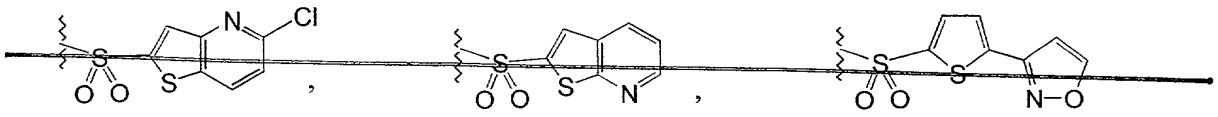
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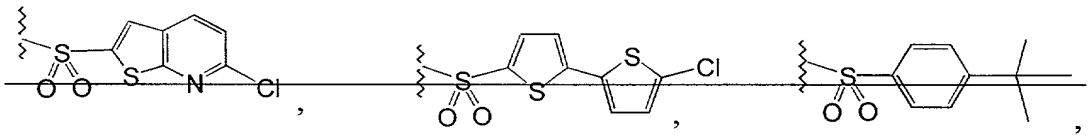
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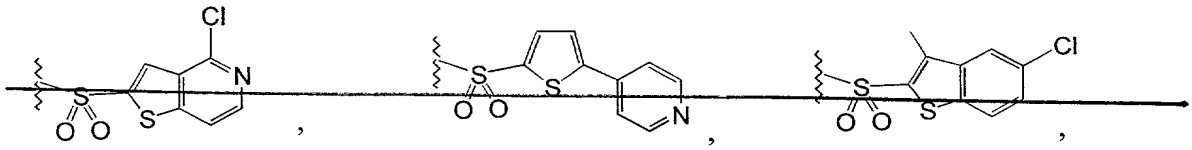
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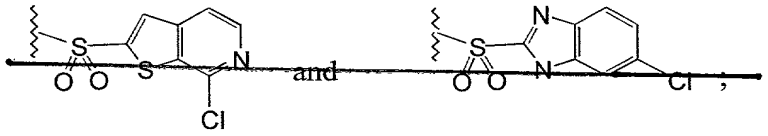
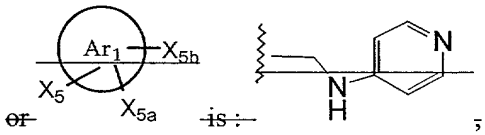

and


or ~~is :~~ ;

~~R_1 is H; and R_2 is a radical selected from the group consisting of:~~